Targeted intra-arterial gemcitabine vs. continuation of IV gemcitabine plus nab-paclitaxel following induction with sequential IV gemcitabine plus nab-paclitaxel and radiotherapy for unresectable locally advanced pancreatic cancer (TIGeR-PaC): A randomized phase 3 multicenter study

Michael J. Pishvaian[1,17], Amer H. Zureikat[2], Charles D. Lopez[3], Kenneth Meredith[4], Emmanuel E. Zervos[5], Hassan Hatoum[6], Ki Y. Chung[7], Daniel J. Berg[8], Antonio Ucar[9], Ripal T. Gandhi[9], Reza Nazemzadeh[10], Nainesh Parikh[11], Paula M. Novelli[2], Brian Kouri[12], Christopher Laing[13], Brian A. Boone[14], Thor Johnson[15], Susan E. Bates[16], Ramtin Agah[17], Karyn A. Goodman[18]

[1]Johns Hopkins University, Washington, DC; [2]University of Pittsburgh Medical Center, Pittsburgh, PA; [3]Oregon Health & Science University, Portland, OR; [4]Sarasota Memorial Health Care System, Sarasota, FL; [5]East Carolina University, Greenville, NC; [6]University of Oklahoma, Oklahoma City, OK; [7]Prisma Health Cancer Institute, Boiling Springs, SC; [8]University of Iowa, Iowa City, IA; [9]Miami Cancer Institute, Miami, FL; [10]Levine Cancer Institute, Charlotte, NC; [11]Moffit Cancer Center, Tampa, FL; [12]Wake Forest Baptist Medical Center, Winston-Salem, NC; [13]Sutter Cancer Center, Sacramento, CA; [14]West Virginia University, Morgantown, WV; [15]Medical University of South Carolina, Charleston, SC; [16]Columbia University, New York, NY; [17]RenovoRx, Los Altos, CA; [18]Mount Sinai Health System, New York, NY

BACKGROUND

Prognosis for locally advanced pancreatic cancer (**LAPC**) remains dismal despite advances in cancer therapy.

Local disease control is important in these patients beyond systemic therapies:

- Localized dual-balloon-mediated delivery of intra-arterial gemcitabine (**IAG**) was demonstrated to be safe in this patient population[1]

TIGeR-PaC is an ongoing phase III clinical trial (**NCT03257033**[i]) comparing the efficacy of IAG to the standard-of-care IV gemcitabine/nab-paclitaxel (**GN**) for patients with LAPC.

Measuring survival outcome as the primary endpoint, TIGeR-PaC is composed of 3 phases:

- Induction phase
- Randomized treatment
- Continuation therapy

DESIGN

SCREEN

- LAPC diagnosed within 6 weeks
- ECOG 0-1

INDUCTION

- 3 cycles of GN
- 1 cycle of radiation (per site preference)
  - IMRT 50 Gy in 25 fractions with concurrent capecitabine, or
  - SBRT 33 Gy in 5 fractions

RANDOMIZED TREATMENT

Patients without progressive disease (**PD**) receive:

- IAG (8 bi-weekly treatments), or
- GN (4 cycles)

CONTINUATION THERAPY

Per investigator's preference, patients without PD receive:

- GN (until PD), or
- Capecitabine (until PD)

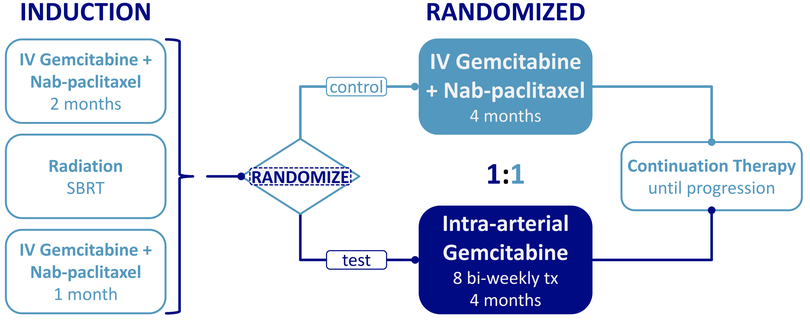
SURVIVAL

Patients with PD at any point post-randomization are followed for survival only

- 1° endpoint is overall survival; 80% power to detect a hazard ratio of 0.6 between both arms

OVERVIEW

The phase III clinical trial, TIGeR-PaC[i], is investigating the benefits of IAG compared to SoC IVG in LAPC patients



- Decision to remove IMRT radiation due to observed differences in toxicity vs. SBRT

[1]Rosemurgy AS, Ross SB, Vitulli PL, Malek R, Li J, Agah R. Safety Study of Targeted and Localized Intra-Arterial Delivery of Gemcitabine in Patients with Locally Advanced Pancreatic Adenocarcinoma. *J Pancreat Cancer*. 2017;3(1):58-65. Published 2017 Aug 1. PMID: 30631844

[i]ClinicalTrials.gov

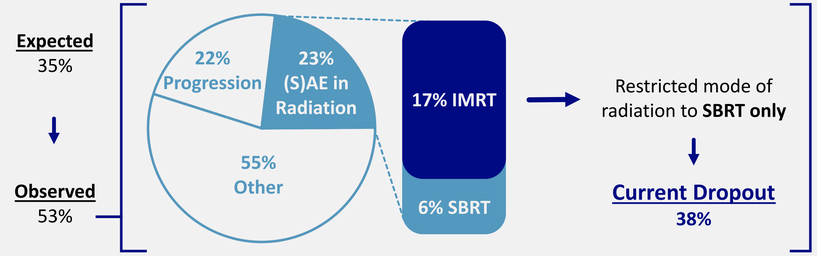
UPDATE/CURRENT

ENROLLMENT

As of September 1, 2022:

- **189** patients enrolled

INDUCTION DROPOUT



We modified the protocol December 2021 to address disproportional, radiation-associated induction dropout rates in patients receiving IMRT. Following this amendment, our current dropout rate decreased from 53% to 38%.

RANDOMIZATION

As of December 21, 2022:

- **47** patients randomized following induction with SBRT only

SAFETY

There was no difference in adverse event, serious (SAE) or not, between the 2 arms (20% in each), with the most common SAE being gastrointestinal related for both arms.

FUTURE

INTERIM ANALYSIS

Planned at 26 events. As of December 21, 2022, TIGeR-PaC has:

- **25** events